

Cutaneous manifestations of visceral malignancy

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HEBRA (1868) was the first to suggest that pigmentation of the skin might indicate the presence of a visceral cancer. With gathering speed, more and more skin reactions which occur before or concurrently with malignant disease have been observed. Some suspected associations such as the presence of Campbell De Morgan angiomas, which were at one time considered harbingers of cancer, are now recognized as incorrect. The more recent example of such negative evidence is the report (Rhodes, 1970) that seed keratoses on the palms and soles thought by Dobson, Young & Pinto (1965) to occur four times as frequently in patients with cancer, affect 62% of skin patients over 40 and indicate no greater proneness to internal neoplasia.

Many skin changes occur in elderly people in the cancer age and it is important therefore to avoid ascribing normal aging effects or even skin disorders of old age to internal carcinoma when the relationship may only be coincidental. There are, however, many very striking associations between skin lesions and visceral cancer but it is easier to observe them in the rare disorders such as acanthosis nigricans or the sudden sprouting of lanugo hair over the face of an adult (Lyle & Whittle, 1951) than in the everyday complaints of generalized pruritus or urticaria. Unfortunately by the time skin lesions such as acanthosis nigricans have appeared the underlying neoplasm is far advanced and there is no opportunity to alter the natural course of the disease. It is particularly important, therefore, to recognize those conditions which may indicate the precancerous state such as the genetic defect of an internal organ which may develop a neoplastic change at an early age.

Skin markers of intestinal defect

A number of syndromes involving the gastro-intestinal tract have been recognized. Hyperkeratosis of the hands and feet, technically known as tylosis,

has been found in several families to indicate a congenital abnormality of the lower end of the oesophagus, which later developed carcinoma. Howel-Evans *et al.* (1958) described two families who suffered from tylosis, which is usually harmless and trivial, but of forty-eight affected members of the families eighteen developed carcinoma of the oesophagus early in life.

More recently, Shine & Allison (1966) described a family who suffered from mild tylosis of rather late onset together with hiatus hernia and a lower oesophagus lined by gastric mucosa. A carcinoma developed in the first patient to be recognized. The son of this patient, who also had dysphagia, was treated by prophylactic removal of an oesophageal stricture. The tylosis in this family was so mild that, had it not been looked for, it would have been missed.

Peutz-Jeghers syndrome

Moving a little further down the gastro-intestinal tract, hereditary polyposis of the small intestine may be associated with pigmentation on the lips, the oral mucosa and sometimes on the fingers (Fig. 1) and the umbilicus. This, the Peutz-Jeghers syndrome, is rarely associated with malignancy in the small intestine (Peutz, 1921; Jeghers, McKusick & Katz, 1949). The pigmented skin changes occur in infancy and may fade at puberty, leaving only the oral pigmentation which persists throughout life. The pigmented freckles on the face are more profuse than usual freckles and involve the red margin of the lips. It is important to emphasize that in the Peutz-Jeghers syndrome polyposis is mainly in the small intestine and symptoms usually arise from haemorrhage or intussusception. Malignant change has been recorded (Kutscher *et al.*, 1959) but more recent reviewers (Dormandy, 1957; Morson, 1962; McKusick, 1962) of the evidence of malignant change in the polyps have come to the conclusion that the great majority are hamartomas and that the

subsequent course of those patients said to have malignant change has contradicted the diagnosis of carcinoma. One recent report (Williams & Knudsen, 1965) claims to be the first to describe a true malignant change in a polyp in the duodenum, with metastasis. Whilst it is true that the risk of malignancy in the small intestine is low, many of these patients do have polyps in the stomach and colon which do not have such a benign course (Dormandy, 1957). Pigmented macules on the lips do not always indicate gastro-intestinal polyposis and there have been a number of instances reported (Calnan, 1960; Belisario, 1965) in which no gastro-intestinal abnormality was found.

Familial polyposis of the colon

This is a far more dangerous disease. Malignancy will occur in 50% of those with symptoms (Dukes, 1958), but fortunately in some families those with polyposis may be indicated by a variety of skin and subcutaneous markers. Gardner and his associates (1951, 1953) described the syndrome of polyposis and subcutaneous bony tumours of the maxilla, the mandible and cranial bones. This syndrome now bears his name. There are now some seventy-five reported examples of this condition, 30% of them with carcinoma (Jones & Cornell, 1966).

Other authors have recorded a variety of subcutaneous benign tumours such as lipoma (Laberge, Saver & Mayo, 1957), osteoma (Weiner & Cooper, 1955), desmoid tumours and epidermoid cysts (Oldfield, 1954; Staley, 1961), which have appeared prior to colonic symptoms. Polyps occur only in those with skin lesions, which therefore serve a useful purpose in indicating those at risk. Dawborn and his colleagues (1962) considered that the likelihood of malignancy in the colonic polyps of Gardner's syndrome was so great that co ectomy in early adult life was justified. They based their opinion on fifty-six patients with Gardner's syndrome of whom eighteen were dead at the average age of 33 as a result of cancer of the colon and rectum. A recent report of familial polyposis (Weston & Wiener, 1967) includes, as well as the sebaceous cysts, pigmented lesions on the surface of the chest and back. The Cronkhite and Canada syndrome is associated with skin and gut changes but does not cause malignant disease (Cronkhite & Canada, 1955).

Acanthosis nigricans

Acanthosis nigricans was the first true dermatosis associated with malignancy; it is the condition which, if found in an adult, denotes that the patient has or will shortly have an adenocarcinoma. One cannot improve on the description of Pollitzer who, in 1890, noted the combination of increased pigmentation and hypertrophy which gives rise to a

dark, velvety thickening of the skin. This occurs constantly on the neck, axillae and groins and frequently round the nipples and umbilicus. Pedunculated papillomas and flat warts arise in the flexures. Velvety thickening of the palms is a useful confirmatory sign (MacKenna, 1957) and the mucous membranes of the mouth and anus are usually involved by warty overgrowths.

Curth, who has done more than anyone to recognize acanthosis nigricans, has emphasized that 90% of the carcinomas underlying the disorder are in the abdomen and 61% arise from the stomach (Curth, 1943; Curth, Hilberg & Machacek, 1962). Invariably the growth is highly malignant and rapidly fatal. Only temporary regression of the acanthosis has followed removal of a primary tumour. The obscure relationship between acanthosis nigricans and a neoplasm can best be demonstrated by a case reported in 1964 by Jenner: a woman who had acanthosis nigricans underwent laparotomy but evidence of carcinoma in the abdomen and pelvis was not found. She died 7 years later and at necropsy was found to have secondary nodules in the liver and in the lungs, and a possible primary in the body of the pancreas.

Seborrhoeic warty lesions

An occasional variant of acanthosis nigricans is the predominance of seborrhoeic wart-like lesions with minimal or absent change at the flexures (Sneddon & Roberts, 1962; Curth *et al.*, 1962; Gougerot & Duperrat, 1942). Some years ago I stumbled across two such cases in men with carcinoma of the stomach. The second of them, a man of 58, was referred for treatment of warts on the arms and legs. He had noticed an increase in the number and size of the warts over a period of 6 months. His only other complaint was lack of energy. The warty growths were distributed in profusion over the front and back of all the limbs but the trunk was spared and, in particular, there were no changes in the mouth, axillae and groins. The warts varied in size from a few mm to 1 cm and in appearance were indistinguishable from seborrhoeic warts. Interspersed between them were café-au-lait pigmented macules. He did not complain of dyspepsia but, because of the similarity of this man's warts to those in the earlier case, a barium meal examination was carried out which showed a filling defect, later proved by laparotomy to be due to an adenocarcinoma of the stomach. At the time I was not aware that this condition had previously been described by a French surgeon, Ulysse Trelât, some time before his death in 1890. The association is well known on the Continent and is called the sign of Trelât (Belisario, 1965; Ronchese, 1965).

During the last year a case was demonstrated to

PLATE 1



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3



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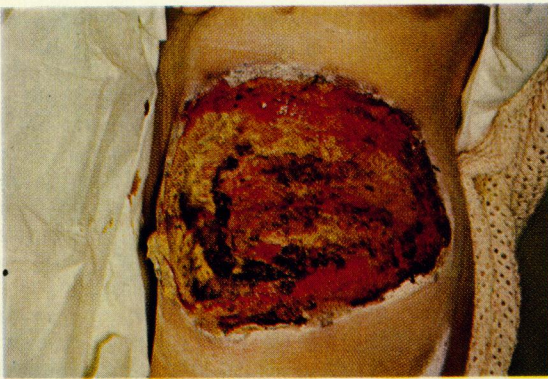
FIG. 1. Pigmentation of fingers in Peutz-Jeghers syndrome.

FIG. 2. Acanthosis nigricans in a patient with cranioma of stomach.

FIG. 3. Dilatation of nail fold capillaries in dermatomyositis.

FIG. 4. Bowen's disease.

6a



6b



7

FIG. 6. Skin necrosis in association with neoplasm. (a) Before treatment, (b) after 10 days of prednisolone.

FIG. 7. Tylosis.

The figure in the bottom right hand corner is to the paper by Hugh C. Dillon (see p. 642) and illustrates typical streptococcal lesions located on the lower extremity of a child with impetigo. Honey-coloured, crusted lesions as well as vesicles are present. (Reproduced by permission of the *American Journal of Diseases of Children*.)

the St John's Society of Dermatology of a widespread papular, scaly eruption associated with a carcinoma of the prostate. In some ways the lesions resemble the generalized seborrhoeic wart-like patches of the incomplete form of acanthosis nigricans (Rhodes, 1970, personal communication).

Much confusion has arisen in the past because a pigmented acanthosis of the flexures occurs as a harmless genetic abnormality in children. This appears soon after birth or before puberty, and juvenile acanthosis nigricans is not related to neoplasia. An even greater source of confusion arises from the pigmentation and pedunculated skin tags which may occur in the axillae and perineum of obese patients, a condition termed pseudo-acanthosis nigricans (Arguelles-Casals, 1949) (Fig. 2). This is comparatively common. We found six examples in 18 months in our own department (Tighe, 1960). The absence of mucous membrane changes, the limited area of acanthosis, and the usual state of obesity served to distinguish this pseudo-acanthosis. It has also been described in endocrine abnormalities such as congenital lipodystrophic diabetes and acromegaly (Brubaker, Levan & Collipp, 1965). There are also occasional reports of acanthosis nigricans without a neoplasm. For instance it has been seen after massive doses of nicotinic acid (Tromovitch, Jacobs & Kern, 1964), after stilboestrol (Katzenellenbogen, 1956) and very, very rarely in patients in whom neoplasm has not been found even at necropsy (*British Medical Journal*, 1966). A recent review of ninety patients with this diagnosis by Brown & Winkelmann (1968) underlines the absence of clinical distinction between the types of acanthosis nigricans. The age of the patient is most important and it is a reasonably safe assumption that if acanthosis nigricans is seen in persons over 40 a neoplasm is responsible.

Dermatomyositis

It is probable that dermatomyositis, the symptom complex of a skin rash (Fig. 3) mainly on the areas of the body exposed to light, muscle weakness and fever, is the end-product of several mechanisms. Its association with malignancy has been known for 50 years (Stern, 1916). From the practical point of view there are a number of questions which need to be answered. First how probable is it that there is an underlying carcinoma? Secondly is it possible that, though dermatomyositis is present, the carcinoma has not yet developed and, therefore, prophylactic treatment might be instituted if one knew where to look? Thirdly, is there a way of differentiating carcinomatous dermatomyositis from forms not so related? Figures of its incidence vary. Arundell and his colleagues (1960) showed that 50% of their patients over 40 with dermatomyositis had an under-

lying neoplasm and this figure was also quoted by Batschwarov & Minkov (1968) in a survey of eighteen cases seen in Bulgaria. I cannot agree with Logan *et al.* (1966) who in a follow-up of sixty-three patients state they have gained the impression that the association of malignancy in dermatomyositis is only a chance occurrence. In our own department in Sheffield, six out of twenty-three patients have had neoplasms, five out of six males and only one out of seventeen females. This sex discrepancy has not been noticed by others but it may be purely chance. It should be emphasized that dermatomyositis in children is not associated with malignancy.

The speed with which dermatomyositis may come on can be most frightening. The most recent example I have seen was in a 68-year-old shop-owner who had felt entirely well until 6 weeks before attending hospital. He had then generally become weak and had found trouble lifting himself out of a chair and difficulty in getting upstairs. It is perhaps worth mentioning that many cases of dermatomyositis are mistakenly diagnosed as hysteria because the muscle weakness may come on so suddenly and in the absence of neurological signs a true diagnosis may be missed. Within 2 weeks of the onset of the weakness he developed intermittent oedema of his eyelids and face and an erythematous rash on the face and hands. On admission to hospital the physical signs and history suggested a diagnosis of dermatomyositis and investigation of transaminases showed that his SGOT was 1000 m.i.u./ml, his creatine phosphokinase 4120 m.i.u./ml and his serum aldolase 54.5. X-ray of chest demonstrated multiple neoplastic deposits and he also had a bony secondary in his spine. Necropsy showed a poorly differentiated squamous cell carcinoma arising from the lower right bronchus.

The skin eruption usually precedes the recognition of a neoplasm by about 6 months, but the interval may be as long as 7 years. It can also occur after treatment of the carcinoma (Calvert & Neale, 1965). To date it is impossible to distinguish the patients with an underlying neoplasm but it has been noted that more neoplasms will be found if they are diligently sought. The likely primary sites are stomach, breast, bronchus and ovary but malignant conditions of the reticulo-endothelial system may also give rise to dermatomyositis (Curtis, Blaylock & Harrell, 1952). It is generally assumed that some form of hypersensitivity is responsible since skin reactions have been found to extracts of tumour cells (Curtis, Heckaman & Wheeler, 1961; Grace & Dao, 1959) and complement fixation tests have also been positive to tumour tissue (Copeman & Alexander, 1967). This work has been further expanded and a rising titre of complement-fixing antibody was shown in the serum of a patient who had a carcinoma of the bladder and in another patient blast cell trans-

formation occurred in a white cell culture exposed to an extract of his own tumour (Alexander & Forman, 1968).

An interesting observation was made by Howell in 1965: a patient with dermatomyositis 9 months after mastectomy for carcinoma underwent hypophysectomy for secondary metastasis, after which the dermatomyositis rapidly remitted.

It should be emphasized that the dermatomyositis with carcinoma is entirely different from the myopathy which the late Lord Brain (1963) described. The muscles are destroyed in dermatomyositis, there is no reaction in response to drugs and the tongue is not smooth and red as in myopathy.

Figurate erythema

In contrast to the poor prognosis of dermatomyositis, the recognition of an association between a figurate erythema and carcinoma is sometimes of benefit to the patient (Gammell, 1952; Purdy, 1959; Summerly, 1964). It is likely that such skin reactions are merely a non-specific change caused most frequently by bacterial or fungus infections or by sensitivity to drugs (Shelley & Hurley, 1960; Shelley 1962) and the association with neoplasm is unusual. In a review of 113 patients with persistent erythema, diagnosed as erythema perstans, White & Perry (1969) found only seven patients in whom there was a relationship between malignancy and the erythema perstans, no more than in a control group suffering from psoriasis. However, it is easy to lose the unusual case in a welter of statistics. Two more patients with erythema gyratum repens associated with carcinoma have just been described (Thomson & Stankler, 1970). They stress that erythema gyratum repens has an appearance which has been described so often previously of the graining of wood and that it may change from hour to hour, and in this way may be differentiated from many other cases of fixed erythema. Having had the opportunity of seeing a case of my colleague Dr Church (Shammy, 1963), I am convinced that an eruption which has these characteristic serpiginous bands of erythema and superficial scaling which change in a few days should be fully investigated for a neoplasm. This is one of the few of the skin markers which, if the carcinoma is discovered in time, is likely to lead to a permanent cure.

Vascular lesions

Vascular changes which may indicate neoplasm have been well described (Forman, 1952). The onset of a fixed erythema-like lupus erythematosus in a patient past middle age, particularly a man, should direct attention to possible carcinoma of the bronchus. The telangiectases so often found in liver disease may also occur with carcinoma of the bronchus. Attention has been drawn recently to an

association between digital ischaemia and malignant disease. Hawley and his colleagues (1967) described six middle-aged women who presented either with a typical Raynaud's phenomenon or with gangrene of the fingers. All the patients succumbed within 18 months of the onset of the vascular lesions and in several the neoplasm was not found until necropsy. The authors recommended that patients who suddenly develop Raynaud's disease and in whom the accepted causes have been excluded should undergo the fullest investigation for neoplasia.

More dynamic vascular changes are seen with carcinoid tumours. In the patients I have seen the flushing attacks have not been dramatic but the ultimate red telangiectatic and bronzed face is characteristic. Associated with flushing may be over-secretion of tears which tends to occur particularly with bronchial carcinoid. Sometimes there may even be erythematous plaques with central necrosis and scarring associated with carcinoid (Bean & Fusaro, 1968). Carcinomatous pressure on blood vessels, particularly the superior vena cava, can give rise to an unusual clinical picture of angio-oedema of the face which may be mistaken for contact dermatitis; the eyelids swell, there may be blepharitis and crusting. This superior vena cava syndrome was well described by Swanson *et al.* (1968) in a case of bronchogenic carcinoma.

Bowen's disease

In 1959, Graham & Helwig observed that patients suffering from Bowen's disease were more likely to develop carcinoma of an internal organ than the general population. Until that time the chronic intra-epidermal neoplasm which Bowen (1912) described, and which can simulate psoriasis or eczema (Fig. 4), had been regarded as a relatively harmless condition which could occasionally give rise to a squamous carcinoma of the skin. Other observers have confirmed Helwig's findings (Epstein, 1960; Peterka, Lynch & Goltz, 1961), and it is probable that between one-third and one-half of patients with Bowen's disease on the covered parts of the body will develop an internal carcinoma in 5–10 years. Graham & Helwig (1961) considered that arsenic might be the carcinogen responsible and the similarity between Bowen's disease and arsenical keratosis certainly supports the theory that arsenic may be the common factor. Two of my own patients with Bowen's disease who developed carcinoma had a history of arsenical medication for psoriasis and epilepsy many years previously. Of nine patients with Bowen's disease under my care, five have since developed cancer. A discovery, therefore, of Bowen's disease on the trunk should initiate a careful search for an internal neoplasm, particularly if there is a history of arsenical medication.

Ichthyosis

Ichthyosis is such a common congenital abnormality that when observed in an adult (Fig. 5) it is a natural assumption that it has been there since birth. However Ronchese (1943) drew attention to the onset of ichthyosis some 11 months before a patient died from Hodgkin's disease. Since that time there have been about thirty cases in the literature (Van Dijk, 1963), most of whom have suffered from Hodgkin's disease or lymphomas; occasionally carcinoma has been mentioned. I am sure that the scanty reports in the literature do not reflect the actual incidence



FIG. 5. Acquired ichthyosis in association with carcinoma.

of the condition. In 1955 I described four patients who developed ichthyosis about a year before there was evidence of lymphadenoma, and I have seen three examples in the last year, two with advanced carcinoma of the breast and one in whom the skin condition aided the diagnosis. This was a 68-year-old woman who for 18 months had felt tired and weak and had suffered from mild generalized pruritus. On examination she was found to have a scaly ichthyotic change on the legs and abdomen which she maintained was of recent origin. The only other physical abnormality was slight enlargement of the liver. A low grade fever, iron deficiency anaemia and a raised ESR were the only abnormal findings. On the basis of the acquired ichthyosis, a liver biopsy was performed which showed Hodgkin's disease.

Pruritus

Generalized pruritus is caused in many ways and neoplasia accounts for such a small proportion of

cases, that it is difficult to refute the possibility of coincidence. Nevertheless itching may precede Hodgkin's disease by several years and less frequently it may be a forerunner of carcinoma (Rothman, 1958). A recent report records that nine of thirty-four patients with supposed senile pruritus had an underlying malignant condition (Rajka, 1966) and Cormia (1965) described five patients with carcinoma whose first symptom was itching.

Dermatitis herpetiformis

Of more value is the discovery of a bullous eruption indistinguishable from dermatitis herpetiformis. Such eruptions have been found with carcinoma of the vulva (Bogrow, 1909), carcinoma of the uterus (Hartzell, 1918), chorion carcinoma (Elliott, 1938), hydatidiform mole (Tillman, 1950), and carcinoma of the ovary (Tobias, 1951).

Rather larger bullous erythema multiforme-like rashes have occurred after deep X-ray therapy for neoplasm (Arnold, 1949; Mazzini & Blasi, 1953): the eruption presumably indicates an allergic reaction to the necrotic tumour cells. Recently, I have seen a generalized erythematous eruption, similar to a drug sensitivity, which occurred 3 weeks after radiation treatment of a carcinoma of the cervix. One of the most curious examples of this group occurred within the last year. A woman who had carcinoma of the breast with metastases had been treated with thiopeta. She developed an area of phagedaenic ulceration on the left flank which continued to extend despite antibiotics and local applications (Fig. 6a). There was no evidence of agranulocytosis. A biopsy suggested a vascular reaction of the arteritic type rather than infection and she was then given prednisolone. Within a few days the spread of the ulceration ceased and healing began (Fig. 6b), being complete in 2 months.

Pemphigoid eruptions

As pemphigoid, the bullous disorder of the elderly, and carcinoma occur in the same age-group it is not surprising that they are sometimes reported in the same patient; but in some it is more than a chance association (Forman, 1960; Gold, 1961). A woman with malignant melanoma, shown at the Royal Society of Medicine in 1961 (Marks, 1961), had a blistering eruption which varied in severity with the presence of the primary and later with secondary deposits of melanoma. On another occasion, pemphigoid appeared coincidentally with acanthosis nigricans in a patient with carcinoma of the cervix (Ive, 1963).

It is my impression that pemphigoid associated with neoplasia affects the mucous membrane more than usual and in a patient with carcinoma of the stomach the changes in the eyes and mouth were

similar to the scarred lesions of mucous membrane pemphigoid. Similar instances have been reported in patients with carcinoma of the bronchus and, perhaps even more interestingly, in a patient whose pemphigoid eruption cleared after the removal of glands infiltrated with an anaplastic carcinoma (Gresson, 1964). Carton & Vanhoutte (1965) have described scarring lesions of the eye in a patient with carcinoma of the stomach. Nevertheless, the subject has recently been reviewed by Parsons & Savin (1968) and one can but agree with their review of the literature that the association between pemphigoid and malignant neoplasms may be coincidental and is nothing like as well proven as some of the other skin markers of malignancy.

Cancer of the pancreas

To date there is no specific eruption which pinpoints a neoplasm in a particular organ. Two curious changes may occur in carcinoma of the pancreas, however, and these are worthy of mention since such carcinomas are so difficult to diagnose.

Graciansky (1967) drew attention to the association of nodular relapsing panniculitis (Weber Christian syndrome) with pancreatic disease, and he described a woman who for 6 months suffered from fever, eosinophilia and subcutaneous nodules which broke down to discharge an oily substance. Malignancy was found on liver biopsy and a primary lesion in the pancreas was demonstrated at necropsy. He found a total of 13 cases in the literature in which nodules, fever, eosinophilia and joint symptoms were proved at necropsy to be due to pancreatic carcinoma.

In 1967 my colleagues Church & Crane, described a woman who suffered from recurrent attacks of erythematous sheets of scaling epidermis which at times became necrotic. The areas involved were the thighs, trunk and arms. The appearance was similar to that of a superficial burn. She also had a red tongue and mild diabetes. Although the eruption was controllable with prednisolone, her general course was downhill. The eruption was so similar to that of a patient described by Becker, Khan & Rothman in 1942, who had an islet cell carcinoma of the pancreas, that a tentative diagnosis of this syndrome was made whilst the patient was still alive. Necropsy showed that she had a carcinoma of the islet cells of the pancreas and thus this very curious eruption appears to have been a specific one.

Porphyria

The only other occasion on which a skin eruption can indicate a neoplasm of a particular site is when porphyria is associated with a hepatoma. The onset of a light sensitive bullous eruption with porphyria in an elderly person with no previous family history of porphyria may indicate such a tumour.

Cutaneous metastases

These occur remarkably seldom. The most recent survey by Reingold (1966) showed thirty-two examples in 2300 necropsies of male cancer patients, and a previous report recorded fifty-eight in 2298 (Gates, 1937). Carcinoma of the lung is the likeliest tumour to metastasize to the skin. The painless nodules in the dermis are usually simple to diagnose but occasionally carcinoma of a sweat gland can cause difficulty.

I have had to omit much that is known, and numerous other rare skin changes in visceral carcinoma have been described in greater detail by others (Belisario, 1965; Cormia & Domonkos, 1965), but I have attempted to illustrate the conditions which are recognizable and which have a fairly close correlation with malignancy. With regard to saving the patient's life, the early recognition of these changes is as yet unrewarding but some progress is being made.

References

- ALEXANDER, S. & FORMAN, L. (1968) Dermatomyositis and carcinoma. A case report and immunological investigation. *British Journal of Dermatology*, **80**, 86.
- ARGUELLES-CASALS, D. (1949) Papillary and pigmentary dystrophy, acanthosis nigricans—type frequent in Negro race. *Medicina latina (Habana)*, **8**, 249.
- ARNOLD, H.L., JR (1949) Erythema multiforme following high voltage Roentgen therapy. Review of literature and report of three cases. *Archives of Dermatology*, **60**, 143.
- ARUNDELL, F.D., WILKINSON, R.D. & HASERICK, J.R. (1960) Dermatomyositis and malignant neoplasms in adults. *Archives of Dermatology*, **82**, 772.
- BATSCHEWAROV, B. & MINKOV, D. (1968) Dermatomyositis and carcinoma. A study based on an 18 year follow-up in Bulgaria. *British Journal of Dermatology*, **80**, 84.
- BEAN, S.F. & FUSARO, R.M. (1968) Unusual manifestations of the carcinoid syndrome. Report of a case. *Archives of Dermatology*, **98**, 268.
- BECKER, S.W., KHAN, D. & ROTHMAN, S. (1942) Cutaneous manifestations of internal malignant tumours. *Archives of Dermatology and Syphilology*, **45**, 1069.
- BELISARIO, J.C. (1965) Some cutaneous manifestations associated with internal cancer. *Australian Journal of Dermatology*, **8**, 85.
- BOGROW, S.L. (1909) Zur Kasuistik der dermatitis herpetiformis Duhringi. *Archiv für Dermatologie und Syphilis*, **98**, 327.
- BOWEN, J.T. (1912) Precancerous dermatoses: a study of 2 cases of chronic atypical epithelial proliferation. *Journal of Cutaneous Diseases including Syphilis*, **30**, 241.
- BRAIN, R. (1963) The neurological complications of neoplasms. *Lancet*, **i**, 179.
- BRITISH MEDICAL JOURNAL (1966) Clinicopathological Conference. **2**, 1642.
- BROWN, J. & WINKELMANN, R.K. (1968). Acanthosis nigricans. Study of 90 cases. *Medicine*, **47**, 33.
- BRUBAKER, M.M., LEVAN, N.E. & COLLIPP, P.J. (1965) Acanthosis nigricans and congenital total lipodystrophy. *Archives of Dermatology*, **91**, 320.
- CALNAN, C.D. (1960) Peutz-Jeghers syndrome. *Transactions of the St John's Hospital Dermatological Society*, **44**, 58.

- CALVERT, H.T. & NEALE, G.J.E. (1965) Dermatomyositis following treatment of cancer. *Postgraduate Medical Journal*, **41**, 371.
- CARTON, F.X. & VANHOUTTE, M. (1965) Dermite Bullense Mucosynechiante et Cancer de l'estomac. *Bulletin de la société française de dermatologie et de syphiligraphie*, **72**, 848.
- CHURCH, R.E. & CRANE, W.A.J. (1967) A cutaneous syndrome associated with islet-cell carcinoma of the pancreas. *British Journal of Dermatology*, **79**, 284.
- COPEMAN, P.W.M. & ALEXANDER, S. (1967) Dermatomyositis. Adenocarcinoma of male breast. Detection of antibodies to the neoplasm in the serum. *Proceedings of the Royal Society of Medicine*, **60**, 183.
- CORMIA, F.E. (1965) Pruritus, an uncommon but important symptom of systemic carcinoma. *Archives of Dermatology*, **92**, 36.
- CORMIA, F.E. & DOMONKOS, A.N. (1965) Cutaneous reactions to internal malignancy. *Medical Clinics of North America*, **49**, 655.
- CRONKHITE, L.W. & CANADA, W.J. (1955) Generalised gastro-intestinal polyposis. An unusual syndrome of polyposis pigmentation, alopecia and onychodystrophia. *New England Journal of Medicine*, **252**, 1011.
- CURTH, H.O. (1943) Cancer associated with acanthosis nigricans. Review of literature and report of case of acanthosis nigricans with cancer of breast. *Archives of Surgery*, **47**, 517.
- CURTH, H.O., HILBERG, A.U. & MACHACEK, G.E. (1962) The site and histology of the cancer associated with malignant acanthosis nigricans. *Cancer*, **15**, 364.
- CURTH, H.O., TOVELL, M.M. & JANOVSKI, N. (1962) Malignant acanthosis nigricans associated with endourethral adenocarcinoma. *Bulletin of the Sloane Hospital for Women, New York City*, **8**, 141.
- CURTIS, A.C., BLAYLOCK, H.C. & HARRELL, E.R., JR (1952) Malignant lesions associated with dermatomyositis. *Journal of the American Medical Association*, **150**, 844.
- CURTIS, A.C., HECKAMAN, J.H. & WHEELER, A.H. (1961) Study of the auto-immune reaction in dermatomyositis. *Journal of the American Medical Association*, **178**, 571.
- DAWBORN, J.K., FERGUSON, J. & STANISTREET, R.H. (1962) Familial polyposis coli and multiple sebaceous cysts and osteomas. Gardner's syndrome. *Australasian Annals of Medicine*, **11**, 195.
- DOBSON, R.L., YOUNG, M.R. & PINTO, J.S. (1965) Palmar keratoses and cancer. *Archives of Dermatology*, **92**, 553.
- DORMANDY, T.L. (1957) Gastro-intestinal polyposis with microcutaneous pigmentation (Peutz-Jeghers Syndrome). *New England Journal of Medicine*, **256**, 1093, 1141, 1186.
- DUKES, C.E. (1958) Cancer control in familial polyposis of the colon. *Diseases of the Colon and Rectum*, **1**, 413.
- ELLIOTT, J.A. (1938) Bullous dermatoses of toxic origin. Report of a case involving association with chorion-carcinoma. *Archives of Dermatology*, **37**, 219.
- EPSTEIN, E. (1960) Association with Bowen's disease with visceral cancer. *Archives of Dermatology*, **82**, 349.
- FORMAN, L. (1952) Skin manifestations of malignant disease. *British Medical Journal*, **2**, 911.
- FORMAN, L. (1960) Pemphigoid occurring with carcinoma of rectum. *Proceedings of the Royal Society of Medicine*, **53**, 563.
- GAMMELL, J.A. (1952) Erythema gyratum repens. Skin manifestations in patient with carcinoma of breast. *Archives of Dermatology*, **66**, 494.
- GARDNER, E.J. (1951) Genetic and clinical study of intestinal polyposis. Predisposing factor for carcinoma of colon and rectum. *American Journal of Human Genetics*, **3**, 167.
- GARDNER, E.J. & RICHARDS, R.C. (1953) Multiple cutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis. *American Journal of Human Genetics*, **5**, 139.
- GATES, O. (1937) Cutaneous metastases of malignant disease. *American Journal of Cancer*, **30**, 718.
- GOLD, S.C. (1961) Pemphigoid with malignant melanoma. *Proceedings of the Royal Society of Medicine*, **54**, 226.
- GOUGEROT, H. & DUPERRAT, B. (1942) Dermatose verruqueuse 'monitrice' d'un cancer viscéral. *Annales de dermatologie et de syphiligraphie*, p. 193.
- GRACE, J.T. & DAO, T.L. (1959) Dermatomyositis in cancer. *Cancer (Philadelphia)*, **12**, 648.
- GRACIANSKY, P. DE (1967) Weber-Christian syndrome of pancreatic origin. *British Journal of Dermatology*, **79**, 278.
- GRAHAM, J.H. & HELWIG, E.B. (1959) Bowen's disease and its relationship to systemic cancer. *Archives of Dermatology*, **80**, 133. (1961) *Ibid.*, **83**, 738.
- GROSSON, C. (1964) Bullous eruptions. Pulmonary neoplasms. *British Journal of Dermatology*, **76**, 346.
- HARTZELL, M.B. (1918) Dermatitis herpetiformis: its etiology and relationship to certain members of the bullous group of diseases. *Journal of Cutaneous and Genito-urinary Diseases including Syphilis*, **36**, 497.
- HAWLEY, P.R., JOHNSTON, A.W. & RANKIN, J.T. (1967) Association between digital ischaemia and malignant disease. *British Medical Journal*, **2**, 208.
- HEBRA, F. (1868) *Journal of Cutaneous Medicine*, **36**, 501.
- HOWEL-EVANS, W., MCCONNELL, R.B., CLARKE, C.A. & SHEPPARD, P.M. (1958) Carcinoma of the esophagus with keratosis palmaris et plantaris (Tylosis). *Quarterly Journal of Medicine*, **27**, 413.
- HOWELL, R. (1965) Dermatomyositis with carcinoma relieved by hypophysectomy. *British Journal of Dermatology*, **77**, 163.
- IVE, F.A. (1963) Metastatic carcinoma of cervix with acanthosis nigricans, bullous pemphigoid and hypertrophic pulmonary osteoarthropathy. *Proceedings of the Royal Society of Medicine*, **56**, 910.
- JEGHERS, H., MCKUSICK, V.A. & KATZ, K.H. (1949) Generalised intestinal polyposis and melanin spots of the oral mucosa, lips and digits. Syndrome of diagnostic significance. *New England Journal of Medicine*, **241**, 993.
- JENNER, F.J.V. (1964) Acanthosis nigricans. *British Journal of Dermatology*, **76**, 485.
- JONES, E.L. & CORNELL, W.P. (1966) Gardner's syndrome: review of the literature and report of a family. *Archives of Surgery*, **92**, 287.
- KATZENELLENBOGEN, I. (1956) Acanthosis nigricans. *Harefuah*, **50**, 241.
- KUTSCHER, A.H., ZEGARELLI, E.V., RANKOW, R.M., MERCANDANTE, L.J. & KUPFERBERG, N. (1959) Peutz-Jeghers syndrome. Follow-ups on patients reported in the literature. *American Journal of Medical Science*, **238**, 180.
- LABERGE, M.Y., SAUER, W.G. & MAYO, C.W. (1957) Soft tissue tumours associated with familial polyposis. *Proceedings of the Staff Meetings of the Mayo Clinic*, **32**, 749.
- LOGAN, R.G., BANDERA, J.M., MIKKELSEN, W.M. & DUFF, I.F. (1966) Polymyositis. *Annals of Internal Medicine*, **65**, 996.
- LYLE, A. & WHITTLE, C.H. (1951) Hypertrichosis lanuginosa acquired type. *British Journal of Dermatology*, **63**, 411.
- MACKENNA, R.M.B. (1957) Discussion of acanthosis nigricans. *Proceedings of the Royal Society of Medicine*, **50**, 276.
- MCKUSICK, V.A. (1962) Genetic factors in intestinal polyposis. *Journal of the American Medical Association*, **182**, 271.
- MARKS, J.M. (1961) Pemphigoid with malignant melanoma. *Proceedings of the Royal Society of Medicine*, **54**, 225.
- MAZZINI, M.A. & BLASI, A.A. (1953) Erupciones Cutaneas Polimorfas Descendadas por Radioterapia Profunda. *Revista argentina de dermatosifilologia*, **37**, 126.

- MORSON, B.C. (1962) Precancerous lesions of upper gastrointestinal tract. *Journal of the American Medical Association*, **179**, 311.
- OLDFIELD, M.C. (1954) Association of familial polyposis of the colon with multiple sebaceous cysts. *British Journal of Surgery*, **41**, 534.
- PARSONS, R.L. & SAVIN, J.A. (1968) Pemphigoid and malignancy. *British Journal of Cancer*, **22**, 669.
- PETERKA, E.S., LYNCH, F.W. & GOLTZ, R.W. (1961) Association between Bowen's disease and internal cancer. *Archives of Dermatology*, **84**, 623.
- PEUTZ, J.L.A. (1921) On a very remarkable case of familial polyposis of the mucous membrane of the intestinal tract and nasopharynx accompanied by peculiar pigmentations of the skin and mucous membranes. *Nederlandsch maandschrift voor geneeskunde*, **10**, 134.
- POLLITZER, S. (1890) *International Atlas of Rare Skin Diseases*. (Ed. by Morris.) Lewis, London.
- PURDY, M.J. (1959) Erythema gyratum repens. Report of a case. *Archives of Dermatology*, **80**, 590.
- RAJKA, G. (1966) Investigation of patients suffering from generalised pruritus, with special reference to systemic disease. *Acta dermato-venereologica*, **46**, 190.
- REINGOLD, I. (1966) Cutaneous metastases from internal carcinoma. *Cancer (New York)*, **19**, 162.
- RHODES, E.L. (1970) Palmar and plantar seed keratoses and internal malignancy. *British Journal of Dermatology*, **82**, 361.
- RONCHESE, F. (1943) Ichthyosiform atrophy of the skin in Hodgkin's disease. *Archives of Dermatology and Syphilis*, **50**, 85.
- RONCHESE, F. (1965) Keratoses, cancer and 'The Sign of Leser Trelat'. *Cancer (New York)*, **18**, 1003.
- ROTHMAN, S. (1958) Pruritus as a symptom of internal disease. *American Practitioner and Digest of Treatment*, **9**, 226.
- SHAMMY, H.K. (1963) Bronchiolar carcinoma presenting as erythema gyratum perstans. *Proceedings of the Royal Society of Medicine*, **56**, 904.
- SHELLEY, W.B. (1962) Auto-immune mechanism in clinical dermatology. *Archives of Dermatology*, **86**, 27.
- SHELLEY, W.B. & HURLEY, H.J. (1960) An unusual auto-immune syndrome. *Archives of Dermatology*, **81**, 889.
- SHINE, L. & ALLISON, P.R. (1966) Carcinoma of the oesophagus with tylosis. *Lancet*, **i**, 951.
- SNEDDON, I.B. (1955) Acquired ichthyosis and Hodgkin's disease. *British Medical Journal*, **1**, 763.
- SNEDDON, I.B. & ROBERTS, J.B.M. (1962) An incomplete form of acanthosis nigricans. *Gut*, **3**, 269.
- STALEY, C.J. (1961) Gardner's syndrome. Simultaneous occurrence of polyposis coli, osteomatosis and soft tissue tumours. *Archives of Surgery*, **82**, 420.
- STERTZ, G. (1916) Polymyositis. *Berliner klinische Wochenschrift*, **53**, 489.
- SUMMERLY, R. (1964) Figurate erythema and neoplasia. *British Journal of Dermatology*, **76**, 370.
- SWANSON, P., SCHORR, W.F., MAGNIN, G.E. & DOVENBARGER, W. (1918) Dermatological manifestations of the S.V.C. syndrome. *Archives of Dermatology*, **98**, 628.
- THOMSON, J. & STANKLER, L. (1970) Erythema gyratum repens: reports of two further cases associated with carcinoma. *British Journal of Dermatology*, **82**, 406.
- TIGHE, S.M. (1960) Pseudo-acanthosis nigricans. *Lancet*, **ii**, 1422.
- TILLMAN, W.G. (1950) Herpes gestationis with hydatidiform mole and chorion epithelioma. *British Medical Journal*, **1**, 1471.
- TOBIAS, N. (1951) Dermatitis herpetiformis associated with visceral malignancy. *Urologic and Cutaneous Review*, **55**, 352.
- TROMOVITCH, T.A., JACOBS, P.H. & KERN, S. (1964) Acanthosis-like lesions from nicotinic acid. *Archives of Dermatology*, **89**, 222.
- VAN DIJK, E. (1963) Ichthyosiform atrophy of the skin associated with internal malignant disease. *Dermatologica*, **127**, 413.
- WEINER, R.S. & COOPER, P. (1955) Multiple polyposis of the colon, osteomatosis and soft tissue tumours: report of a familial syndrome. *New England Journal of Medicine*, **253**, 795.
- WESTON, S.D. & WIENER, M. (1967) Familial polyposis associated with a type of soft tissue lesion (skin pigmentation): report of 3 cases and a review of the literature. *Diseases of the Colon and Rectum*, **10**, 311.
- WHITE, J.W. & PERRY, H.O. (1969) Erythema perstans. *British Journal of Dermatology*, **81**, 64.
- WILLIAMS, R.C. JR (1959) Cancer accompanying dermatomyositis. *Annals of Internal Medicine*, **50**, 1174.
- WILLIAMS, J.P. & KNUDSEN, A. (1965) Peutz-Jeghers syndrome with metastasizing duodenal carcinoma. *Gut*, **6**, 179.

Erratum

Postgraduate Medical Journal, **46**, October 1970.

The paper 'The definition and evaluation of skills required to obtain a patient's history of illness: the use of videotape recordings' was written by J. Anderson, J. L. Day, M. A. C. Dowling and K. W. Pettingale, not J. Anderson, J. L. Day, M. A. C. Dowling and K. W. Dowling as printed on the cover. We would like to apologise to Dr Pettingale for this error.